IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of:

CROMACK, Keith R. et al.

Serial No.: 10/526,755

Filed: November 14, 2005

For: MEDICAL DEVICE HAVING HYDRATION INHIBITOR

Art Unit: 1615

Examiner: Azpuru, Carlos A.

Confirmation No.: 6909

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPEAL BRIEF

Dear Sir:

This appeal brief is submitted pursuant to the Notice of Appeal filed August 16, 2010.

REAL PARTY IN INTEREST

The real party in interest is Abbott Cardiovascular Systems, Inc., with its primary place of business at 3200 Lakeside Drive, Santa Clara, California 95054. The assignment of the application to Abbott Cardiovascular was recorded at Reel/Frame 019736/0302 on 22 August 2007.

RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences that might have any bearing, direct or indirect, on the Board's decision in this appeal.

STATUS OF CLAIMS

The current status of the claims is:

Claims 1-3, 5-14 and 20-25 are pending.

Claims 1-3, 5-8, 20 and 23-25 are rejected.

Claims 9-14, 21 and 22 are objected to.

No claims are currently withdrawn by the examiner.

Claims 1- 3, 5 - 14 and 20 - 25 and are being appealed and are the subject of this appeal brief.

STATUS OF AMENDMENTS

The claims have never been amended.

SUMMARY OF CLAIMED SUBJECT MATTER

The claimed subject matter is directed to a medical device having an interventional component for delivering one or more beneficial agents, in which a

hydration inhibitor controls delivery of at least one beneficial agent from the device. Independent claim 1, the only independent claim currently on appeal, states:

1. A medical device comprising:

an interventional component to be deployed in a patient;

a beneficial agent to be delivered from the interventional component, the beneficial agent loaded on at least a portion of the interventional component and having a first LogP value; and

an effective amount of a hydration inhibitor associated with the beneficial agent to control delivery of the beneficial agent from the interventional component, the hydration inhibitor having a second LogP value, the second LogP value being greater than the first LogP value.

Support for a medical device having an interventional component to be deployed in a patient can be found at least at page 1, lines 12-20, page 8, lines 7-9 and page 52, lines 7-13.

Support for a beneficial agent loaded on at least a portion of the interventional component having a first logP can be found at least at page 8, lines 15-18, page 9, lines 27-29 and page 50, lines 9-15.

Support for a hydration inhibitor having a second logP that is greater than the logP of the beneficial agent can be found at least at page 8, lines 18-20, page 9, lines 29-32 and page 50, lines 9-15.

Support for the hydration inhibitor controlling the delivery of the beneficial agent can be found at least at page 1, lines 12-15, and page 50, lines 9-15.

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The grounds for rejection to be reviewed in this appeal are:

1. that claim 1-3, 5-8 and 20-25 are anticipated by, and therefore unpatentable under 35 U.S.C. § 102(b) over, Iyer et al., WO 02 062335 ("Iyer") (Evidence Appendix, Exhibit "A").

2. that the specification does not define the values "logP" or "effective amount", presumably a rejection under 35 U.S.C. §112.

ARGUMENT

1. Claims 1-3, 5-8, 20 and 23-25 are patentable over Iyer.

Appellants disagree with the examiner's assertion that Iyer anticipates the present claims. Iyer teaches the use of an extra-vascular matrix or device (also referred to as perivascular in Iyer) for the delivery of drugs for the treatment of neointimal hyperplasia (new proliferation of neointimal cells at the site of damage inside a body lumen such as a blood vessel). Examples of the Iyer invention include teachings in paragraph 25 (method of doing so extravascularly or perivascularly *i.e.* from outside the vascular or graft lumen), and paragraph 26 (implantable prosthetic device placed on the outer surface of the vessel or graft).

It is true that Iyer includes a disclosure of a stent with a polymeric carrier containing rapamycin and dexamethasone. This disclosure, however, is of the prior art, and Iyer teaches away from the use of this prior art combination, at least at page 44, paragraph 127. In this paragraph, Iyer compares elution of a drug set from the perivascular device of the '335 patent application with the elution of the same drug set from an intravascular coated stent: "In contrast to a dexamethasone eluting stent, perivascular delivery does not inhibit endothelial cell regeneration and acts directly on fibroblasts and smooth muscle cells." (Iyer page 44, last full sentence) This is an important result, as restenosis, or repeat blockage of a blood vessel, can occur from growth of fibroblasts and smooth muscle cells at a damaged vessel site, while new endothelial cells are needed to repair the lesion in the vessel.

Iyer is also lacking in the elements that deal with hydrophobicity and hydrophilicity. The present claims require that log P of the first beneficial substance being delivered be lower than the log P of a second substance, the hydration inhibitor. (Note that the hydration inhibitor can also be a beneficial substance.) The examiner

only states that because of certain absences in the description of the present invention, logP is "of questionable value" in limiting and/or defining the claim. Please see part 2 below, addressing this assertion by the examiner.

It is unclear how the examiner finds that Iyer anticipates the present claims. One possibility is that the examiner finds that the logP is an inherent aspect of a substance, and therefore cannot be used to make that substance novel. However, the claims here are not directed to a new composition of matter as different over a previous composition of matter, based on its log P. Applicants are aware that log P is a characteristic of a substance that can be easily determined, and have used this characteristic as part of their currently claimed invention. The present application uses the ratio of a particular characteristic of a first substance and of a second substance to define an aspect of the invention: log P of the beneficial as compared to log P of the hydration inhibitor, to define the relative amounts of each to use. In other words, the present claim 1 takes information about the hydrophilicity of substance one, measured by its log P, and the same type of information about substance two, measured by its log P, and compares these two numbers to find a preferred ratio of amount of the two substances to be delivered on the interventional component in order to control delivery of the first substance. *See* claim 1, listed above. This use of inherent characteristics to create an invention is the same as the use of other easily determined characteristics. An inherent characteristic alone might not be novel, but the use of the characteristic in a comparison certainly can be novel and non-obvious.

2. Claims 1-3, 5-8, 20 and 23-25

In what appears to be a 35 USC §112 rejection, the examiner states that the present application does not teach certain elements of the claims: that the specification does not define logP and does not define effective amount. Applicants clearly have covered these issues in the specification. First, easily found and understood on page 50, paragraph 3, of the specification, applicants teach the meaning of the terms P and log P. The P, or log P as it is usually expressed, relates to the hydrophilicity or hydrophobicity of a substance. "The phrases 'relatively less hydrophilic' and 'relatively more hydrophilic' as used herein relate to the partitioning in water compared to partitioning in another substance." (p. 50, lines 16-18). Applicants then referred the

reader to the well known and well used CRC Handbook of Chemistry and Physics, which explains that the octanol-water partition coefficient, log P, is a widely used parameter for correlating biological effects of organic substances. (p. 50, lines 18-20).

Log P is determined by placing a substance in a biphasic solution wherein one phase is octanol-rich and the other is water-rich. In many cases, the first phase is pure octanol, and the second phase is pure, de-ionized water. When the solution reaches equilibrium, the substance is distributed between the two phases, and the amount in each phase is measured. Log P is defined as the ratio of the equilibrium concentration of the substance in the octanol-rich phase to that in the water-rich phase. (page 50, lines 20-25) Log P correlates to the hydrophilicity of a substance, with long non-polar substances having a high log P (less hydrophilic), and small compounds with highly polar groups having a low log P (more hydrophilic). (page 50, line 25 through page 51, line 11)

In the Advisory Action, the examiner has stated that the application does not provide what base log P is in: "the log P value is of questionable value since no base number or power is defined." This is untrue. It is very well known that a log is in base 10 unless otherwise designated. What the examiner means by the "power" not being defined is not understood, as "log P".

CONCLUSION

The examiner has failed, as a matter of law, to set forth a case of anticipation of claims 1-3, 5-8, 20 and 23-25 by Iyer. Nor has the examiner set forth a case of violation of §112. Appellants therefore respectfully request that the Board reverse the examiner's rejection(s) and order that the application proceed to issue.

Date: October 18, 2010

Respectfully submitted,

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CLAIMS APPENDIX

The claims on appeal are:

1. A medical device comprising:

an interventional component to be deployed in a patient;

a beneficial agent to be delivered from the interventional component, the beneficial agent loaded on at least a portion of the interventional component and having a first LogP value; and

an effective amount of a hydration inhibitor associated with the beneficial agent to control delivery of the beneficial agent from the interventional component, the hydration inhibitor having a second LogP value, the second LogP value being greater than the first LogP value.

2. The device according to claim 1, wherein the beneficial agent is selected from a group consisting of antithrombotics, anticoagulants, antiplatelet agents, anti-lipid agents, thrombolytics, antiproliferatives, anti-inflammatories, agents that inhibit hyperplasia, smooth muscle cell inhibitors, antibiotics, growth factor inhibitors, cell adhesion inhibitors, cell adhesion promoters, antimitotics, antifibrins, antioxidants, antineoplastics, agents that promote endothelial cell recovery, antiallergic substances, viral vectors, nucleic acids, monoclonal antibodies, antisense compounds, oligonucleotides, cell permeation enhancers, pro-drugs and combinations thereof.

3. The device according to claim 2, wherein the beneficial agent is selected from the group of indomethacin, phenyl salicylate, B-estradiol, vinblastine, ABT-627, testosterone, progesterone, paclitaxel, cyclosporin A, vincristine, carvedilol, vindesine, dipyridamole, methotrexate, folic acid, thrombospondin mimetics, estradiol, dexamethasone, metrizamide, iopamidol, iohexol, iopromide, iobitridol, iomeprol, iopentol, ioversol, ioxilan, iodixanol, iotrolan and pro-drugs, analogs, derivatives, or combinations thereof.

5. The device according to claim 1, wherein the hydration inhibitor is selected from a group consisting of beneficial agents, polymeric materials, markers, additives, and combinations thereof.

6. The device according to claim 1, wherein the hydration inhibitor is a second beneficial agent.

7. The device according to claim 6, wherein the second beneficial agent is selected from a group consisting of antioxidants, antithrombotics, anticoagulants, antiplatelet agents, anti-lipid agents, thrombolytics, antiproliferatives, anti-inflammatories, agents that inhibit hyperplasia, smooth muscle cell inhibitors, antibiotics, growth factor inhibitors, cell adhesion inhibitors, cell adhesion promoters, antimitotics, antifibrins, antioxidants, antineoplastics, agents that promote endothelial cell recovery, antiallergic substances, viral vectors, nucleic acids, monoclonal antibodies, antisense compounds, oligonudeotides, cell permeation enhancers, radiopaque agents markers and combinations thereof

8. The device according to claim 7, wherein the second beneficial agent is selected from a group consisting of paclitaxel, rapamycin, rapamycin derivatives, pimecrolimus, everolimus, fenofibrate, carvedilol, taxoteres, tacrolimus, butylated hydroxytoluene, butylated hydroxyanisole, vitamin E, danazol, probucol, tocopherols, tocotrienols, ABT-578, ABT-627 and analogs, derivatives, or combinations thereof.

9. The device according to claim 6, wherein the hydration inhibitor is associated with the first beneficial agent as a layer of the second beneficial agent at least partially covering the first beneficial agent.

10. The device according to claim 9, further comprising an outer layer of a third beneficial agent, the third beneficial agent having a third LogP value.

11. The device according to claim 10, wherein the third LogP value is less than the second LogP value.

12. The device according to claim 10, wherein the third beneficial agent is the same as the first beneficial agent.

13. The device according to claim 6, wherein the hydration inhibitor is associated with the first beneficial agent as a mixture of the second beneficial agent with the first beneficial agent.

14. The device according to claim 1, wherein the hydration inhibitor is associated with the beneficial agent as a mixture of the hydration inhibitor and the beneficial agent.

20. The device according to claim 1, further comprising a layer of polymeric material on at least a portion of a surface of the interventional component, the beneficial agent at least partially loaded onto the layer of polymeric material.

21. The device according to claim 20, wherein the layer of polymeric material has a zwitterionic pendant group.

22. The device according to claim 21, wherein the layer of polymeric material has a phosphoryl choline pendant group.

23. The device according to claim 20, wherein the hydration inhibitor controls a delivery of the beneficial agent from the layer of polymeric material.

24. The device according to claim 1, wherein the interventional component is selected from the group consisting of a stent, graft, stent-graft, valve, filter, coil, staple, suture, guidewire, catheter, and catheter balloon.

25. The device according to claim 1, wherein the first LogP value Is at least about 0.5 units less than the second LogP value.

EVIDENCE APPENDIX

Attached hereto are the following Exhibits:

A. Iyer, et al., WO2002/062335